In the Claims

Please amend claims 1, 17, 18, 36-47, 49-51, and 53-55 so that they read as shown below. Please cancel Claims 33 and 34, without prejudice. A copy of the amended claims that shows the changes that were made in this response is attached. The remaining claims are unchanged in this response. The status of the claims is as follows:

- Claims 1-32 and 35-56 are pending.
- Claims 33 and 34 have been cancelled.
- New Claim 56 is submitted to replace Claim 33, with changes relating to formalities.
- Claims 1, 17, 18, 36-47, 49-51, and 53-55 are amended herein.
- Claims 27, 31, 32, and 35 were amended once previously.

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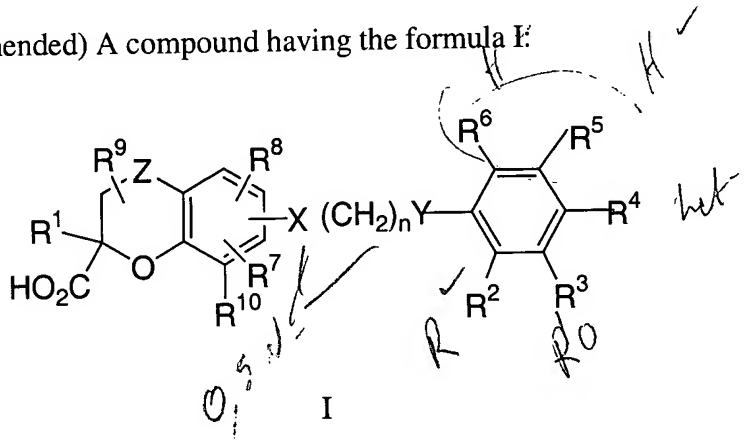
1. (Amended) A compound having the formula I:



I

or a pharmaceutically acceptable salt or prodrug thereof, wherein:

Z is selected from the group consisting of CH_2 and C=O;

R^1 is selected from the group consisting of H, -OH, C_{1-7}alkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, -OC_{1-3}alkyl, -OC_{2-3}alkenyl, -OC_{2-3}alkynyl, F, Br, Cl, and Ar, wherein alkyl, alkenyl, alkynyl, -Oalkyl, -Oalkenyl and -Oalkynyl are linear or branched and are optionally substituted with (a) 1-7 halogen

atoms, (b) 1-3 groups independently selected from (i) -OC_{1-3}alkyl, which is optionally substituted with 1-5 halogen atoms, and (ii) phenyl, which is optionally substituted with 1-3 groups independently selected from halogen, C_{1-5}alkyl and -OC_{1-3}alkyl, said C_{1-5}alkyl and -OC_{1-3}alkyl being linear or branched and optionally substituted with 1-5 halogens, or (c) a mixture of (a) and (b);

Ar is Aryl, wherein Aryl is in each instance optionally substituted with 1-5 substituents independently selected from (a) halogen, (b) C_{1-5}alkyl, (c) C_{2-5}alkenyl, (d) C_{2-5}alkynyl, (e) -OC_{1-5}alkyl, (f) –OC_{2-5}alkenyl, (g) –OC_{2-5}alkynyl, (h) -SO_xC_{1-5}alkyl, (i) -$SO_xNR^aR^b$, (j) –SO_xphenyl, (k) –$C(O)C_{1-3}$alkyl, and (l) -$C(O)NR^aR^b$, wherein in each instance, each alkyl, alkenyl and alkynyl is linear or branched and is optionally substituted with (a) 1-5 halogen atoms, (b) 1-2 groups independently selected from -OC_{1-3}alkyl, which is linear or branched and is optionally substituted with 1-5 halogens, or (c) a mixture thereof, and wherein phenyl is optionally substituted with 1-3 substituents independently selected from halogen, C_{1-3}alkyl, and C_{1-3}alkoxy, wherein C_{1-3}alkyl and C_{1-3}alkoxy are linear or branched and are optionally substituted with 1-5 halogens;

x is selected from 0, 1 and 2;

Aryl is a carbocyclic 6-10 membered monocyclic or bicyclic aromatic ring system;

Hetcyc is a 5- or 6-membered saturated or partly saturated monocyclic heterocycle having 1-4 heteroatoms independently selected from N, S, and O in the perimeter of the ring, wherein N may optionally be NR^a and S may optionally be SO or SO_2;

Benzoheterocycle comprises a 5 or 6-membered heterocyclic ring which may be saturated, partly unsaturated or aromatic, and a benzene ring, wherein said heterocyclic ring and said benzene ring are fused together, wherein said heterocyclic ring comprises 1-3 heteroatoms independently selected from O, S, and N in the perimeter of the ring, where N may optionally be NR^a, and S may optionally be SO or SO_2;

R^a and R^b are independently selected from the group consisting of H, C_{1-5}alkyl, C_{2-5}alkenyl, C_{2-5}alkynyl, -$C(O)C_{1-5}$alkyl, -$C(O)C_{2-5}$alkenyl, -$C(O)C_{2-5}$alkynyl, SO_xC_{1-5}alkyl, SO_xphenyl, $SOxNR^dR^e$, -$C(O)NR^dR^e$, halogen, and phenyl, wherein in all instances, alkyl, alkenyl, and

alkynyl are linear or branched and are optionally substituted with (a) 1-5 halogen atoms, (b) 1-3 groups independently selected from -OCH_3, -OCF_3 and phenyl, or (c) a mixture thereof, wherein phenyl in all occurrences is optionally substituted with 1-3 substituents independently selected from halogen, C_{1-3}alkyl, and C_{1-3}alkoxy, said C_{1-3}alkyl and C_{1-3}alkoxy being linear or branched and optionally substituted with 1-5 halogens;

R^d and R^e are independently selected from H, C_{1-5}alkyl, C_{2-5}alkenyl, C_{2-5}alkynyl, and phenyl, wherein said alkyl, alkenyl, and alkynyl are linear or branched and are optionally substituted with (a) 1-5 halogen atoms, (b) 1-3 groups independently selected from -OCH_3, -OCF_3 and phenyl, or (c) a mixture thereof, wherein phenyl in all occurrences is optionally substituted with 1-3 substituents independently selected from halogen, C_{1-3}alkyl, and C_{1-3}alkoxy, said C_{1-3}alkyl and C_{1-3}alkoxy being linear or branched and optionally substituted with 1-5 halogens;

X and Y are independently selected from the group consisting of O, S, SO, SO_2, NR^a and CH_2;

O, S, N No way

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n is an integer from 1-6;

R^2, R^3, R^5, R^6, R^7, R^8, R^9 and R^{10} are independently selected from the group consisting of H, halogen, C_{1-7}alkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, -OH, -OC_{1-5}alkyl, -OC_{2-5}alkenyl, -OC_{2-5}alkynyl, -$C(O)C_{1-5}$alkyl, -$C(O)C_{2-5}$alkenyl, -$C(O)C_{2-5}$alkynyl, -$C(O)OC_{1-5}$alkyl, -$C(O)OC_{2-5}$alkenyl, -$C(O)OC_{2-5}$alkynyl, -$OC(O)C_{1-5}$alkyl, -$OC(O)C_{2-5}$alkenyl, -$OC(O)C_{2-5}$alkynyl, Ar, -OAr, -C(O)Ar, -C(O)OAr, -OC(O)Ar, C_{3-8}Cycloalkyl, -OC_{3-8}Cycloalkyl, -SO_xC_{1-5}alkyl, -$SO_xNR^aR^b$, -SO_xAr, and -$C(O)NR^aR^b$, wherein in each instance, each alkyl, alkenyl, and alkynyl is linear or branched and is optionally substituted with (a) 1-5 halogen atoms, (b) 1-2 groups independently selected from -OC_{1-3}alkyl groups which are linear or branched and are optionally substituted with 1-5 halogens, (c) 1 group Ar or C_{3-6}Cycloalkyl, or (d) a mixture of more than one of (a), (b) and (c);

R^4 is selected from the group consisting of Benzoheterocycle, C_{3-8}Cycloalkyl, Hetcyc, -OC_{3-8}Cycloalkyl and R^c, with the proviso that if R^4 is R^c, then either (1) R^1 is not H, and no more than one of R^2, R^6, and R^{10} is alkyl, or (2) R^2 is Cl, Br or F, and R10 is not alkyl;

wherein Benzoheterocycle, C_{3-8}Cycloalkyl, Hetcyc and -OC_{3-8}Cycloalkyl are each optionally substituted with 1-3 groups independently selected from halogen, C_{1-5}alkyl, C_{2-5}alkenyl, C_{2-5}alkynyl, -OC_{1-5}alkyl, -OC_{2-5}alkenyl, -OC_{2-5}alkynyl, C_{3-8}Cycloalkyl, -SO_xC_{1-5}alkyl,

$-SO_xNR^aR^b$,$-SO_x$phenyl, $C(O)C_{1-3}$alkyl and $-C(O)NR^aR^b$, wherein in all instances, said C_{1-5}alkyl, C_{2-5}alkenyl , and C_{2-5}alkynyl groups are linear or branched and are optionally substituted with 1-3 halogens, and wherein Hetcyc, $-OC_{3-8}$Cycloalkyl and C_{3-8}Cycloalkyl may optionally have a C_{3-6}-spiro-cycloalkyl substituent on the ring where gem-disubstitution of a ring carbon is possible, wherein the spiro-cycloalkyl group is optionally substituted with 1-2 groups independently selected from methyl, trifluoromethyl, methoxy, trifluoromethoxy and halogen;

wherein R^c is selected from the group consisting of halogen, -OH, $-OSO_2C_{1-8}$alkyl, $-OSO_2C_{3-8}$Cycloalkyl, $-OSO_2$Ar, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, $-OC_{1-8}$alkyl, $-OC_{2-8}$alkenyl, $-OC_{2-8}$alkynyl, and Aryl, wherein said $-OSO_2C_{1-8}$alkyl, C_{1-8}alkyl, C_{2-8}alkenyl, C_{2-8}alkynyl, $-OC_{1-8}$alkyl, $-OC_{2-8}$alkenyl, and $-OC_{2-8}$alkynyl are linear or branched, and are optionally substituted with (a) 1-5 halogens, (b) 1-2 groups independently selected from $-OC_{1-3}$alkyl, which are linear or branched and which are optionally substituted with 1-5 halogens, (c) 1 group selected from Aryl and C_{3-8}Cycloalkyl, or (d) a mixture of one or more of (a), (b) and (c), and Aryl and C_{3-8}Cycloalkyl are each optionally substituted as defined under Ar for Aryl and R^4 for C_{3-8}Cycloalkyl;

or alternatively R^4 and the adjacent substituent R^3 or R^5 may be connected to form a 5- or 6-membered heterocyclic ring that may be saturated, partly unsaturated or aromatic fused to the benzene ring, wherein the 5- or 6-membered fused ring comprises 1-3 heteroatoms independently selected from O, S, and N, where N may optionally be NR^a and S may optionally be SO or SO_2, said fused ring optionally also comprising 1-2 C=O groups in the perimeter of the ring, wherein said 5- or 6-membered heterocyclic fused ring is optionally substituted with 1-2 groups independently selected from R^3.

17. (Amended) A compound as recited in Claim 1, wherein R^4 is R^c, R^1 is selected from the group consisting of -OH, C_{1-7}alkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, $-OC_{1-3}$alkyl, $-OC_{2-3}$alkenyl, $-OC_{2-3}$alkynyl, F, Br, Cl, and Ar, wherein alkyl, alkenyl, alkynyl, -Oalkyl, -Oalkenyl and -Oalkynyl are linear or branched and are optionally substituted with (a) 1-7 halogen atoms, (b) 1-3 groups independently selected from (i) $-OC_{1-3}$alkyl, which is optionally substituted with 1-5 halogen atoms, and (ii) phenyl, which is optionally substituted with 1-3 groups independently selected from halogen, C_{1-5}alkyl and $-OC_{1-3}$alkyl, said C_{1-5}alkyl and $-OC_{1-3}$alkyl being linear or branched and optionally

substituted with 1-5 halogens, or (c) a mixture of (a) and (b); with the proviso that no more than one of R^2, R^6, and R^{10} is alkyl.

18. (Amended) A compound as recited in Claim 1, wherein R^4 is R^c, and R^2 is Cl, Br or F, with the proviso that R^{10} is not alkyl.

36. (Amended) A method for treating or controlling non-insulin dependent (Type 2) diabetes mellitus in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

37. (Amended) A method for treating or controlling hyperglycemia in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

38. (Amended) A method for treating or controlling lipid disorders, hyperlipidemia, or low HDL in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

39. (Amended) A method for treating or controlling obesity in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

40. (Amended) A method for treating or controlling hypercholesterolemia in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

41. (Amended) A method for treating or controlling hypertriglyceridemia in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

42. (Amended) A method for treating or controlling dyslipidemia and/or low HDL cholesterol in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

43. (Amended) A method for treating or controlling atherosclerosis in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

44. (Amended) A method for treating or controlling cachexia in a mammalian patient in need of such treatment which comprises administering to said patient a therapeutically effective amount of a compound of Claim 1.

45. (Amended) A method of treating or controlling one or more diseases, disorders, or conditions selected from the group consisting of (1) non-insulin dependent diabetes mellitus (NIDDM), (2) hyperglycemia, (3) impaired glucose tolerance, (4) insulin resistance, (5) obesity, (6) lipid disorders, (7) dyslipidemia, (8) hyperlipidemia, (9) hypertriglyceridemia, (10) hypercholesterolemia, (11) low HDL levels, (12) high LDL levels, (13) atherosclerosis and its sequelae, (14) vascular restenosis, (15) irritable bowel syndrome, (16) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (17) other inflammatory conditions, (18) pancreatitis, (19) abdominal obesity, (20) neurodegenerative disease, (21) retinopathy, (22) neoplastic conditions, (23) adipose cell tumors, (24) adipose cell carcinomas, such as liposarcoma, (25) prostate cancer and other cancers, including gastric, breast, bladder and colon cancers, (26) angiogenesis, (27) Alzheimer's disease, (28) psoriasis, (29) acne vulgaris, (30) skin diseases modulated by PPAR, (31) high blood pressure, (32) Syndrome X, (33) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, said method comprising the administration of an effective amount of a compound of Claim 1.

46. (Amended) A method of treating or controlling one or more diseases, disorders, or conditions selected from the group consisting of (1) diabetes mellitus, and non-insulin dependent diabetes mellitus (NIDDM), (2) hyperglycemia, (3) impaired glucose tolerance, (4) insulin resistance, (5) obesity, (6) lipid disorders, (7) dyslipidemia, (8) hyperlipidemia, (9) hypertriglyceridemia, (10) hypercholesterolemia, (11) low HDL levels, (12) high LDL levels, (13) atherosclerosis and its sequelae, (14) vascular restenosis, (15) irritable bowel syndrome, (16) inflamatory bowel disease,

including Crohn's disease and ulcerative colitis, (17) other inflammatory conditions, (18) pancreatitis, (19) abdominal obesity, (20) neurodegenerative disease, (21) retinopathy, (22) neoplastic conditions, (23) adipose cell tumors, (24) adipose cell carcinomas, such as liposarcoma, (25) prostate cancer and other cancers, including gastric, breast, bladder and colon cancers, (26) angiogenesis, (27) Alzheimer's disease, (28) psoriasis, (29) acne vulgaris, (30) skin diseases modulated by PPAR, (31) high blood pressure, (32) Syndrome X, (33) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, said method comprising the administration of an effective amount of a compound of Claim 1, and an effective amount of one or more other compounds selected from the group consisting of:

(a) insulin sensitizers; (I) PPARγ agonists; (ii) biguanides; (iii) protein tyrosine phosphatase-1B (PTP-1B) inhibitors; (iv) dipeptidyl peptidase IV inhibitors;

(b) insulin or insulin mimetics;

(c) sulfonylureas;

(d) α-glucosidase inhibitors;

(e) cholesterol lowering agents selected from the group consisting of (i) HMG-CoA reductase inhibitors, (ii) sequestrants, (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPARα agonists, (v) PPARα/γdual agonists, (vi) inhibitors of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitors, and (viii) anti-oxidants;

(f) PPARδ agonists;

(g) antiobesity compounds (anorectics);

(h) an ileal bile acid transporter inhibitor; and

(i) anti-inflammatory agents.

47. (Amended) A method for the treatment or control of one or more conditions selected from hypercholesterolemia, atherosclerosis, low HDL levels, high LDL levels, hyperlipidemia, hypertriglyceridemia, and dyslipidemia, which method comprises administering to a mammalian patient in need of such treatment a therapeutically effective amount of a compound of Claim 1 and a therapeutically effective amount of an HMG-CoA reductase inhibitor.

49. (Amended) The method as recited in Claim 48, wherein the statin is selected from the group consisting of lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, itavastatin, rosuvastatin and rivastatin.

50. (Amended) A method for the treatment or control of one or more conditions selected from inflammatory conditions, inflammatory bowel disease, Crohn's disease, and ulcerative colitis, which method comprises administering to a mammalian patient in need of such treatment a therapeutically effective amount of a compound according to Claim 1.

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51. (Amended) A method for treating or preventing atherosclerosis in a mammalian patient in need of such treatment comprising the administration to said patient of an effective amount of a compound of Claim 1 and an effective amount of an HMG-CoA reductase inhibitor.

53. (Amended) The method as recited in Claim 52, wherein the statin is selected from the group consisting of lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, itavastatin, rosuvastatin and rivastatin.

54. (Amended) A pharmaceutical composition comprising: (1) a compound according to Claim 1, (2) an HMG-CoA reductase inhibitor, and (3) a pharmaceutically acceptable carrier.

55. (Amended) A pharmaceutical composition comprising (1) a compound according to Claim 1, (2) one or more compounds selected from the group consisting of :

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(a) insulin sensitizers; (ii) biguanides; (I) PPARγ agonists; (iii) protein tyrosine phosphatase-1B (PTP-1B) inhibitors, and (iv) dipeptidyl peptidase IV (DP-IV) inhibitors;

(b) insulin or insulin mimetics;

(c) sulfonylureas;

(d) α-glucosidase inhibitors;

(e) cholesterol lowering agents selected from the group consisting of (i) HMG-CoA reductase inhibitors, (ii) sequestrants, (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPARα agonists, (v) PPARα/γdual agonists, (vi) inhibitors of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitors, and (viii) anti-oxidants;

(f) PPARδ agonists;

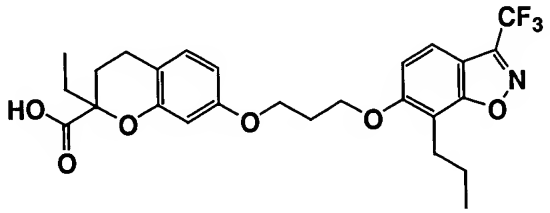
(g) antiobesity compounds (anorectics);

(h) an ileal bile acid transporter inhibitor; and

(i) anti-inflammatory agents; and

(3) a pharmaceutically acceptable carrier.

56. (New) A compound represented by a structure shown below, or a pharmaceutically acceptable salt or prodrug thereof, wherein the structure is selected from the group consisting of:



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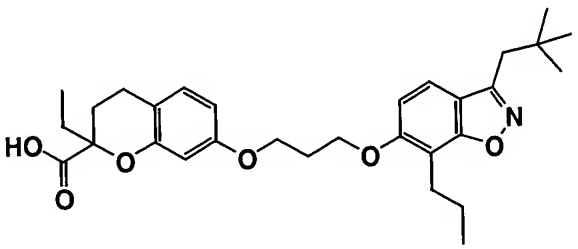

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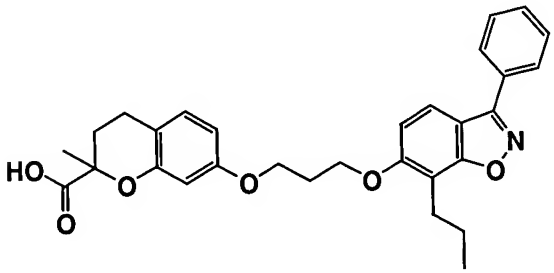

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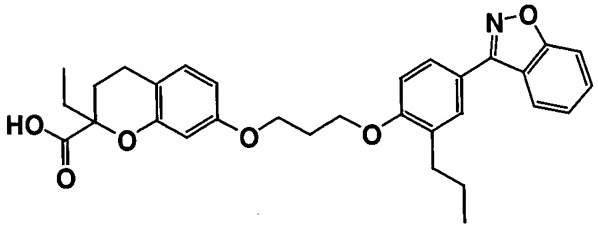

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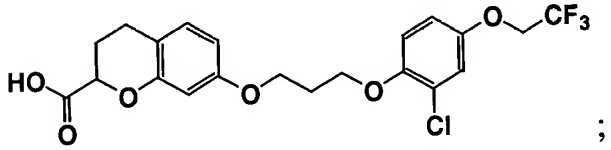

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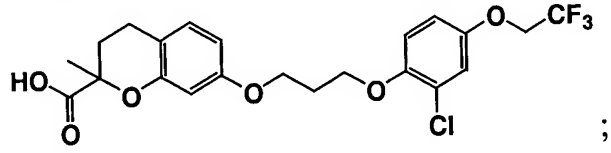

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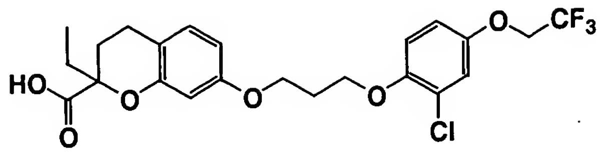
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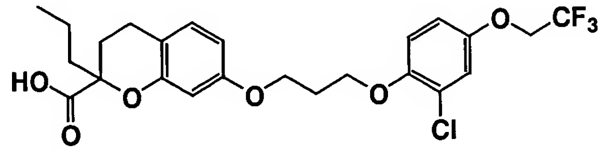
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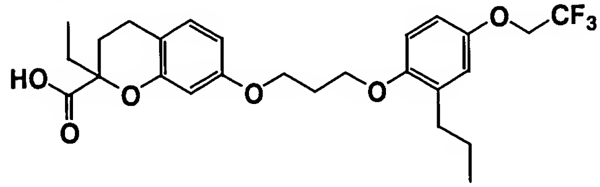
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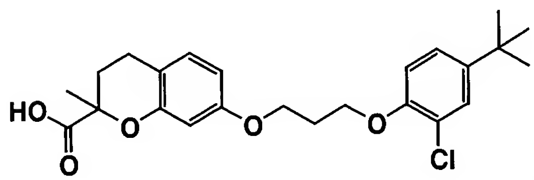
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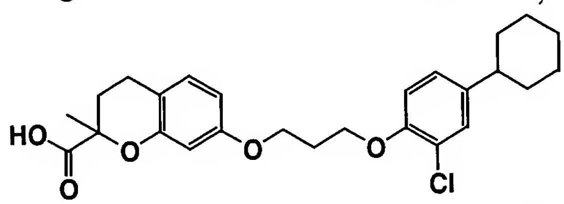
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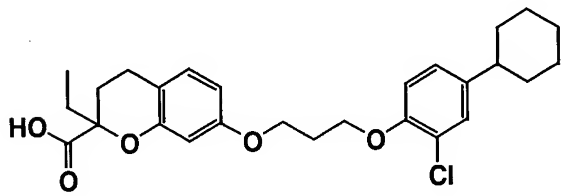
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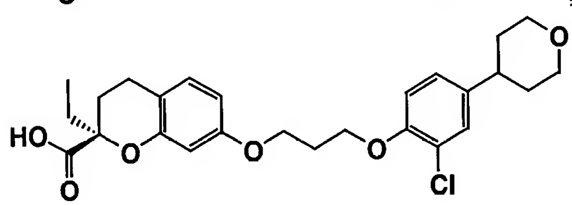
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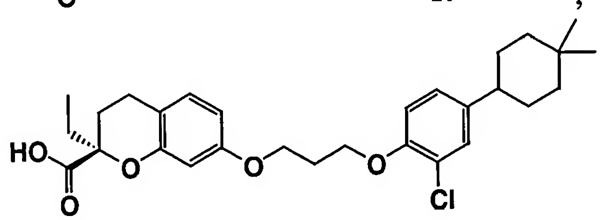
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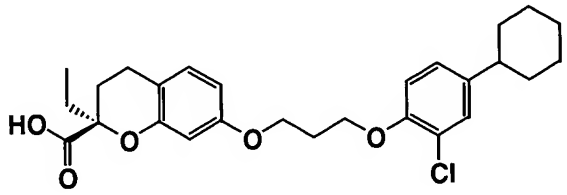
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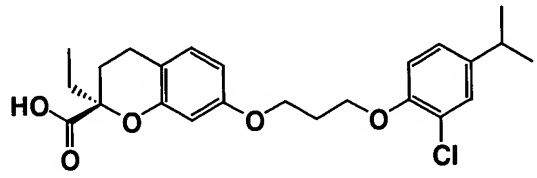
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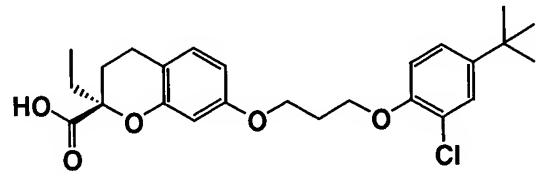
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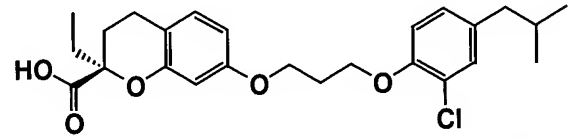
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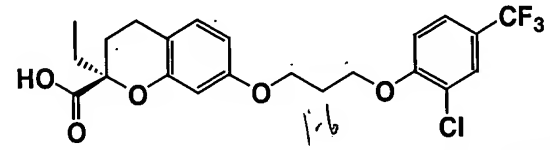
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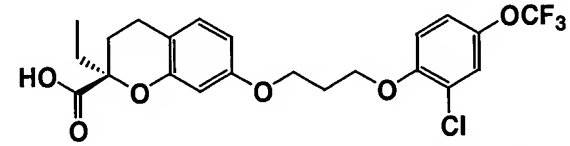
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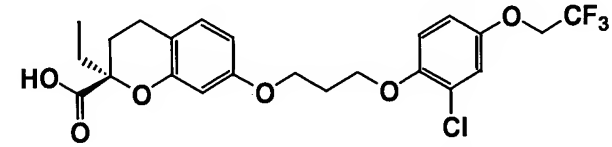
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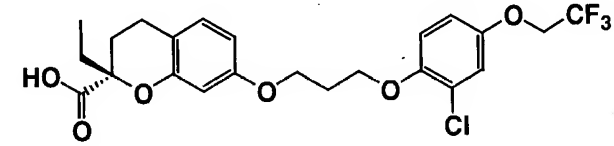
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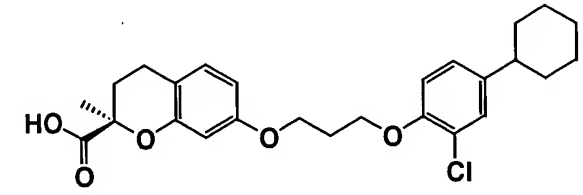
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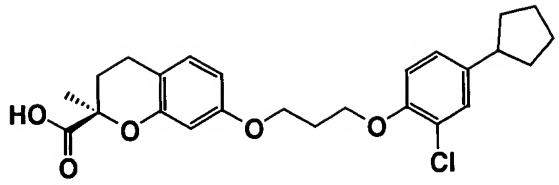
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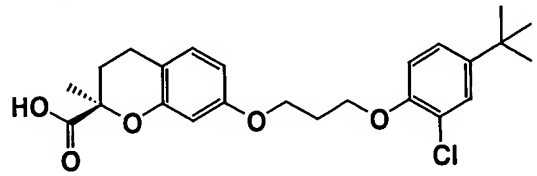
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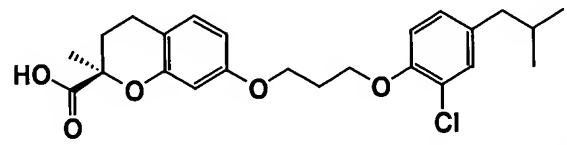
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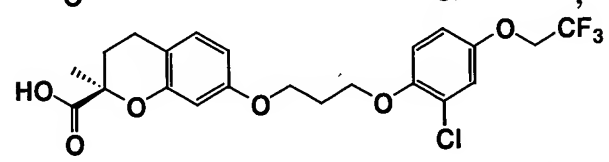
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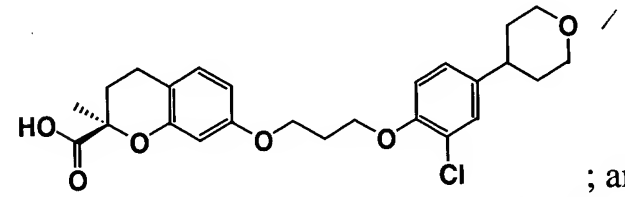
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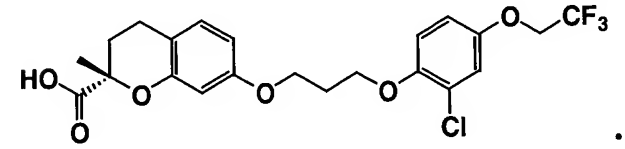
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